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U. S. Army
Chemical Warfare Laboratories
Technical Report

CWLR 2290

Cutaneous Application of 1.1% Malathion Powder to Volunteers

by

Philip S[illegible]

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CUTANEOUS APPLICATION OF 1.1% MALATHION POWDER TO VOLUNTEERS

by

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U. S. ARMY
Chemical Corps Research and Development Command
CHEMICAL WARFARE LABORATORIES
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FOREWORD

This work was authorized under Project 4-08-02-022, Medical Aspects of CW, Subproject 4-08-02-022-03, Clinical Investigation and Treatment of CW Casualties, and OSG-21-88-T208-55, Toxicity Test on Malathion Powder. The work was initiated on 3 July 1958 and completed on 31 July 1958. This report was submitted for publication on 10 April 1959.

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DIGEST

~~This was~~ a pilot study to determine the safety with which 1.1% malathion powder ~~could~~ be used when dusted over a person's entire body. The study also attempted to evaluate troop reaction to frequent dustings. During the entire study, consisting of eight complete cutaneous dustings in a 15-day period, there was no significant cholinesterase depression which could be ascribed to the malathion and there was no evidence of toxicity as determined by daily examination of the men. Troop acceptances of the powder throughout the experiment was good and there was no evidence that nonpowdered personnel objected to the presence of the powdered volunteers. From these studies, it appears that 1.1% malathion could safely be used on a large-scale field trial.

CUTANEOUS APPLICATION OF 1.1% MALATHION POWDER TO VOLUNTEERS

I. INTRODUCTION.

Malathion (0,0-dimethyldithiophosphate of diethylmercaptosuccinate) is an organic phosphate insecticide and pesticide which exerts its effect by inhibiting the enzyme cholinesterase and thereby increasing the concentration of acetylcholine with its subsequent ganglionic and parasympathetic postganglionic stimulation. This agent has been found effective against body lice, including those which have become DDT-resistant. It has a low degree of toxicity in animals as shown by numerous studies.

One group (1) studied inhalation toxicity of malathion in rats and guinea pigs in which all air to the chamber was bubbled through 90% technical malathion for 8 hours/day, 5 days/week, for 2 weeks. There were no fatalities or significant cholinesterase drop, but autopsy revealed coagulation necrosis of alveolar walls and intra-alveolar hemorrhage. An aerosol of 90% technical malathion averaging 5 ppm in air was presented to mice, rats, guinea pigs, and one dog for 8 hours/day, 5 days/week, for 4 weeks, and there were no signs of cholinesterase inhibition; autopsy revealed thickening of the alveolar walls with leukocytic infiltration. This same group applied 90% technical malathion to the clipped abdomen of albino rabbits at 4 cc/kg (applied for 18 hours under rubber binding); there were no abnormalities pre- or post-mortem. Using a concentration of 0.5-1.0 cc/kg daily, there was mortality after the fourth application and this was characteristic of cholinesterase inhibition.

When daily sublethal doses were administered to rats, a cumulative inhibitory action on cholinesterase of all tissues studied was noted (brain, submaxillary gland, plasma); however, the depression in plasma was more pronounced and occurred more rapidly than in other tissues. This signifies that exposure to malathion can be detected by plasma cholinesterase before onset of cholinesterase inhibition in nervous tissue (2). A comparison of the acute oral LD50 (mg/kg) dose of malathion with other insecticides is as follows: malathion, 369-739; DDT, 115; dieldrin, 50-55; chlordan, 590; TEPP, 1.4; parathion, 1.75-5.0 (3). The intraperitoneal LD50 in mg/kg for rats of malathion is 750 and of parathion is 4-20; the percutaneous LD50 (mg/kg) of malathion in rats is over 2500. (2, 4, 5).

Few controlled human studies have been done. In one field survey (6), twelve men (eleven of whom used no personal preventive measures to avoid exposure) used a solution consisting of 1 pint of a 50% emulsion of malathion per 100-150 gallons of water and had an exposure time of 8-9 hours/day for 2-9 days (eight men) or 6 hours/day for 2-13 days (four men). No cholinesterase inhibition was noted. Another study (7) involved eight men wearing absorbent pads (to determine malathion concentration) who worked 6.4 hours/day for 13 days using a spray consisting of 6 pounds of malathion as an emulsifiable concentrate plus 10 pounds of DDT in 1,200 gallons of water. It was estimated that each man received a total exposure of 4,526 mg of malathion or about 3.4 mg/kg/day throughout the entire period. There was an increase in plasma cholinesterase (perhaps a low level of exposure may stimulate the liver to produce additional cholinesterase); no significant decrease in RBC cholinesterase was noted. One report (8) concerns accidental overexposure to malathion in three individuals (one adult and two children), all of whom were hospitalized with symptoms of acute, severe anticholinesterase poisoning. All recovered, but the adult retained residua, consisting of peripheral neuropathy, 2 years after exposure. This indicates that caution must be exercised with this compound, even though it apparently is of low toxicity when compared to other pesticides.

Since some body lice have become DDT-resistant, it may become important to replace DDT by malathion in those areas where lice constitute a health hazard to the troops. Therefore, this is to be a pilot study on a small number of men to determine the safety with which malathion can be tested on troops as a large-scale field trial.

II. PROCEDURE.

Ten volunteers were chosen after a screening consisting of a history and a complete physical examination, including an EKG, red and white blood counts, hemoglobin analysis, urinalysis, and chest X-ray. These volunteers were then instructed to wear the same set of fatigue uniforms during the periods of exposure (including underclothes and socks) throughout the entire experiment. Whenever showers were permitted, the men could wear their civilian clothes after the shower, but the following day they wore the original fatigue uniform. Red-cell (RBC) and plasma cholinesterase control values (two or three) were determined and then repeated daily during the dusting period; the final value was determined 6 days after the last exposure. Cholinesterase values were determined by the Michel method with a microtechnique modification (9). At no time were

the volunteers informed of symptoms which might arise after being exposed to an anticholinesterase agent; however, they were interviewed and examined twice daily by the same medical officer; there was a medical officer on call at all times. Three ounces of a powder consisting of 98.9% pyrophyllite (an inert dust) and 1.1% malathion was applied to the entire body, including hair, axilla, groin, and feet, in early morning immediately after breakfast. During the first week, showers were permitted 8 hours after exposure; the second week, there were no showers and the volunteers were not permitted to change their clothes throughout an 80-hour period. In the third week, the men were dusted twice and did not shower during this time. This terminated the dusting portion of the experiment. During the entire experiment, there were 8 days of actual dusting. All volunteers were told to avoid oily or greasy compounds since malathion is readily absorbed in this type of vehicle.

III. RESULTS.

Cholinesterase values are given in the table. There was no significant change in the plasma values; these values normally have a wide fluctuation. RBC values dropped significantly in all the volunteers on 15 July; however, the following day they returned to normal and the drop was considered *in vitro* due to parathion (a potent cholinesterase inhibitor) contamination in the laboratory refrigerator. The normal values on 16 July were determined without first refrigerating the blood and thereafter all determinations were performed on nonrefrigerated blood. Another decrease in RBC cholinesterase occurred on 28 July; again it returned to normal the following day and this drop can be ascribed to laboratory contamination since these men had had no exposure to malathion for 5 days and the air vents in the laboratory were turned off due to an electricity failure thereby allowing toxics to accumulate in the room. It is important to note that normal nonexposed subjects who had a cholinesterase value determined that day also had a decrease which was significant and which returned to normal the following day. Usually a significant decrease in RBC cholinesterase which is caused by an actual anticholinesterase exposure would require several weeks to 120 days for complete return to normal, although occasionally the values will return to normal in 24-48 hours. The other values for RBC cholinesterase were within normal fluctuation plus laboratory error; statistical analysis of these data for the group revealed no trends which could be correlated with the dusting program. One population was represented by 13 of the 15 days; the other two days were 15 and 28 July (as shown by Tukey's method for determining whether several means belong to the same population).[10] To screen liver function, a BSP (bromsulphthalein) test was performed after the last exposure and there was no significant increase in retention at 45 minutes.

Table

Cholinesterase Values and BSP Retention Values of Individuals Involved in Testing

Date	Cholinesterase values of various subjects																							
	J.B.		J.C.		H.D.		C.H.		J.O.		N.S.		W.S.		R.U.		P.W.		J.Y.		(Duster)		(Duster)		(Duster)	
	RBC	PI	RBC	PI	RBC	PI	RBC	PI	RBC	PI	RBC	PI	RBC	PI	RBC	PI	RBC	PI	RBC	PI	RBC	PI	RBC	PI	RBC	PI
	ΔpH units																									
Control	0.75	1.36	0.79	0.90	0.75	1.25	0.67	0.85	0.76	1.41	0.71	1.2[illegible]	0.67	1.42	0.82	1.30	0.82	0.95	0.82	1.52	[illegible]99	1.52	0.94	1.20	0.81	0.91
Control	0.72	0.93	0.88	1.03	0.78	0.97	0.72	0.80	0.83	0.97	0.76	1.0[illegible]	0.71	1.07	0.86	1.29	0.81	0.83	0.98	1.43	0.98	1.36	0.81	1.13	0.72	1.05
Control	0.73	0.78	0.80	0.86	0.82	0.86	ND	ND	0.74	0.93	0.79	0.9[illegible]	0.77	1.00	0.86	1.24	ND	ND	0.72	1.37	1.08	1.16	0.87	1.07	0.76	0.90
Av control	0.73	1.02	0.82	0.93	0.78	1.03	0.70	0.82	0.78	1.00	0.75	1.07	0.72	1.16	0.85	1.28	0.815	0.89	0.84	1.44	1.02	1.35	0.87	1.13	0.76	0.96
*10 Jul	0.78	1.09	0.78	1.12	0.79	0.97	0.68	1.10	0.95	1.15	0.78	1.1[illegible]	0.77	1.41	0.81	1.49	0.83	1.16	0.85	1.51	0.96	1.60	ND	ND	ND	ND
*11 Jul	0.70	0.72	0.76	0.75	0.83	0.76	0.76	0.79	0.79	0.65	0.73	0.95	0.70	0.91	0.77	1.07	0.73	0.86	0.91	1.16	ND	ND	ND	ND	0.73	0.79
*14 Jul	ND	ND	0.74	0.88	0.77	0.95	0.69	0.91	0.72	[illegible]92	0.78	1.13	0.63	0.97	0.65	1.11	0.64	1.06	0.81	1.29	1.05	1.39	0.92	1.19	ND	ND
*15 Jul	0.57	0.77	0.62	0.81	0.61	0.77	0.54	0.76	0.69	0.71	0.54	1.02	0.49	0.94	0.62	1.10	0.62	0.90	0.55	1.15	ND	ND	ND	ND	0.60	1.17
16 Jul	0.69	0.84	0.76	0.89	0.87	0.88	0.73	0.91	0.83	0.82	0.[illegible]3	1.0[illegible]	0.65	0.97	0.78	1.10	0.74	1.02	0.86	1.26	ND	ND	ND	ND	ND	ND
*17 Jul	0.78	0.78	0.75	0.96	0.82	1.02	0.77	0.87	0.70	0.87	0.81	1.37	0.70	1.09	0.81	1.36	0.71	1.09	0.84	1.33	ND	ND	ND	ND	ND	ND
18 Jul	0.72	0.88	0.64	0.79	0.72	0.88	0.61	1.04	0.80	0.92	0.81	1.25	0.64	1.19	0.65	1.39	0.63	1.12	0.72	1.20	1.11	1.27	ND	ND	0.63	0.89
*22 Jul	0.69	0.80	0.86	1.00	0.76	0.80	ND	ND	0.78	0.95	0.73	1.15	0.71	0.93	0.70	1.30	0.72	1.03	0.85	1.04	ND	ND	ND	ND	ND	ND
*23 Jul	0.72	0.91	0.74	0.94	0.85	0.98	0.64	0.85	0.72	0.86	0.68	1.14	0.64	0.99	0.73	1.62	0.73	1.12	0.73	1.25	ND	ND	ND	ND	0.73	0.97
24 Jul	0.75	1.18	0.82	1.06	0.81	0.95	0.72	1.04	0.75	0.92	0.73	1.30	0.68	1.09	0.75	1.49	0.79	1.20	0.79	1.46	0.92	1.27	ND	ND	0.62	0.96
28 Jul	0.55	0.86	0.67	0.93	0.65	0.78	0.55	0.81	0.66	0.84	0.49	1.01	0.53	0.94	0.59	1.02	0.65	1.16	0.61	1.06	ND	ND	ND	ND	0.55	0.78
29 Jul	0.78	1.05	0.88	1.00	0.81	1.04	0.74	0.9[illegible]	0.[illegible]	0.95	0.72	1.08	0.77	1.07	0.73	1.28	0.73	1.12	0.80	1.39	0.84	1.17	0.91	1.11	0.79	1.09

	BSP retention (45-min) of various subjects												
	J.B.	J.C.	H.D.	C.H.	J.O.	N.S.	W.S.	R.U.	P.W.	J.Y.	(Duster)	(Duster)	(Duster)
	%												
23 Jul	1.9	2.8	8.4	9.3	1.4	2.3	3.7	1.7	10.3	2.6	ND	ND	ND

* Indicates day on which volunteers received malathion powder.

NOTE. Normal cholinesterase values: plasma (PI), 0.60-1.5; ΔpH units, red blood cell (RBC), 0.60-1.9 ΔpH units, normal fluctuation, 0.07 ΔpH units.
BSP retention in 45 min: normal, 0-6%; borderline, 7-11%.

In general, the troops had no subjective complaints. One volunteer developed Pityriasis rosea which was asymptomatic and self-limited; he continued to receive the malathion powder while the exanthem was present. One person complained of a generalized pruritus which was mild and relieved with a shower. Another had an acute exacerbation of Tinea pedis which responded readily to therapy; malathion powder was not applied to his feet. A fourth volunteer developed a large pustule on his anterior abdominal wall on the last day of dusting and had no further exposure to the powder; he has had recurring pustules for several years, some of which required incision and drainage.

Diaphoresis was present among all the volunteers, but this could readily be correlated with the weather which was hot and humid at the time of the experiment. This sweating was not present when the humidity and/or temperature decreased even though the men continued to receive the powder. During this period the relative humidity ranged from 40% to 100%; the temperature ranged from 73.5° to 89.0°F and the temperature of the barracks averaged 2.2°F higher than the outside. Other symptoms which might be caused by an anticholinesterase agent such as headache, eye pain, salivation, difficulty in breathing, abdominal cramps, diarrhea, or muscular weakness, were never present in any volunteer. Physical examination revealed no findings exclusive of diaphoresis; the pupils were never miotic and always reacted to light.

IV. DISCUSSION.

There are two important aspects of this experiment. One is the safety with which malathion powder can be applied to the troops and the other is the troop reaction to continuous dusting. From this pilot study, it appears that 1.1% malathion powder should be relatively innocuous when applied in the manner described. It should be noted that if this powder were to be used in the field, it would probably be applied once or twice during each 30-day period. This time period has been suggested due to the work of Cole, et al. (11), who studied the mortality of DDT-resistant lice exposed to pyrethrins, lindane, and malathion placed in a sleeve around a volunteer's arm. The lice were exposed to each agent at regular intervals up to 3 weeks after the initial treatment, at which time there was still 97% mortality to malathion. Therefore, the exposure of each individual to the powder under actual field conditions would be much less than was present in this experiment, where each person received a dose of 3 ounces of the powder on 8 separate days (24-ounces) in a 15-day period. Following up examinations 6 days after the last exposure revealed no residua or sequelae

of the dusting. The troops reaction to the powder was very satisfactory. Their activity during the day was sedentary, consisting mainly of reading, playing cards, and sleeping. One volunteer played softball several times without untoward effects. An occasional volunteer complained of a "gritty or sandy" sensation in his mouth after being dusted, but this was readily relieved by rinsing his mouth with water. The appetite remained good and the taste of food was not altered; some appetites decreased during the hot and humid weather, but this could not be correlated with the dustings. The most discomfort seemed to arise from the restriction of showers while wearing the same clothes for a prolonged period of time. However, several men noted that the powder actually helped them tolerate the no-bathing period by absorbing the perspiration; they would have welcomed any absorbent powder during this time. Apparently the powder, which is almost odorless, had no effect on other nonexposed volunteers (approximately 20) who slept and lived in the same barracks as the dusted volunteers. Also, one volunteer went to a dance wearing the dusted fatigues and seemingly had no difficulty getting dancing partners. Since the powder was not mosquito-repellant, mosquitos attacked the powder volunteers as readily as the nonpowdered ones, even though the test group slept in dusted clothes.

All volunteers claimed that there would be no personal objection to receiving the powder ever week for a year or more if they thought it would protect them from lice. They also suggested that a mosquito repellant be added to the powder. However, since most repellants are liquids, this at present is not feasible.

There were three enlisted men who were in charge of dusting and they remained asymptomatic throughout the experiment; they never wore protective face masks. There was no significant change in their cholinesterase values. Their only contact with the powder was during the actual dusting procedure which took approximately 10 minutes and during which time they wore fatigue clothes. They thought that most troops could be readily trained to dust themselves under the supervision of a duster and would probably not object to it. One volunteer was in charge of insecticide and rodenticide control in Korea and thought that malathion powder would compare favorably with DDT and lindane as far as troop acceptance was concerned.

V. SUMMARY.

This was a pilot study to determine the safety with which 1.1% malathion powder could be used when dusted over a person's entire body. The study also attempted to evaluate troop reaction to frequent dustings.

10. Tukey, J. W., Comparing Individual Means in the Analysis of Variance, Biometrics 5, 99 (1949).

11. Cole, M. M., Clark, P. H., and Weidhaas D. E., Sleeve Tests With Malathion Powders Against DDT-Resistant Body Lice, J. Econ. Ent. (in press).

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